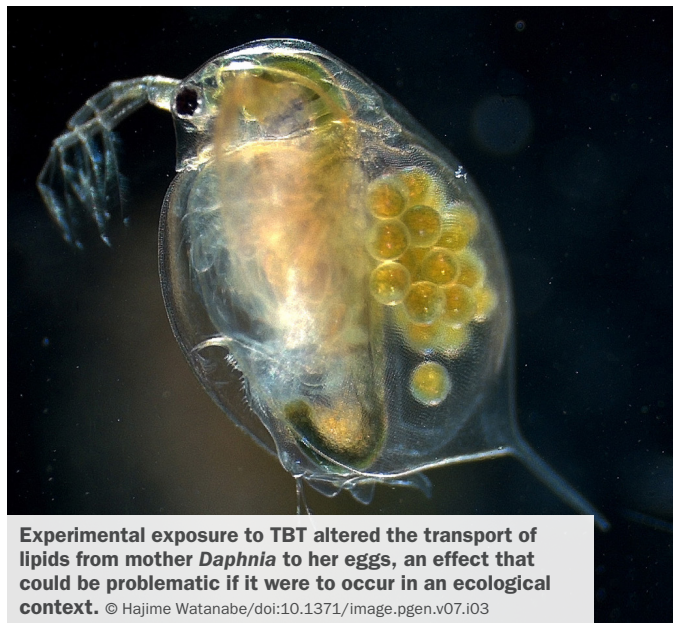


## A Closer Look at Obesogens

### Lipid Homeostasis Disruption in *Daphnia*

Obesogenic chemicals promote weight gain in mammals by altering lipid metabolism, which results in increased fat accumulation.<sup>1</sup> Altered lipid metabolism has been associated with serious health problems, including obesity, diabetes, and an increased risk of cardiovascular disease.<sup>2</sup> However, very little is known about how obesogenic chemicals might affect invertebrate species. In this issue



of *EHP*, researchers suggest that altered lipid transport from the maternal organism to the egg by a known obesogen may be responsible for reproductive problems in *Daphnia magna*, a tiny freshwater crustacean.<sup>3</sup>

In the study, the researchers exposed *Daphnia* to 0.1 µg/L or 1.0 µg/L of the organometallic pollutant tributyltin (TBT). Once used widely as a biocide in paints designed to keep marine invertebrates from sticking to the hulls of ships, TBT was later shown to accumulate in the environment and harm the reproduction and development of aquatic organisms.<sup>4</sup> In marine snails, TBT causes a condition called imposex, in which females develop male sex organs.<sup>5</sup> In mouse studies it also has been shown to increase lipid accumulation and promote weight gain across multiple generations.<sup>6</sup> In 2008 the International Maritime Organization severely restricted its use as a biocide.<sup>4</sup>

*Daphnia*, also known as the water flea, is used widely as a model in ecotoxicology studies.<sup>7</sup> Within the last decade, scientists have started to use *Daphnia* in biomedical research as a surrogate species for genomic responses to environmental stressors.<sup>7</sup> “We wanted to test whether *Daphnia* could be used as an invertebrate model for obesogenic effects,” says senior author Carlos Barata, an ecotoxicologist at the Institute of Environmental Assessment and Water Research in Barcelona, Spain.

Female water fleas typically release a brood of offspring each time they molt (shed their exoskeleton). Between molts, *Daphnia* stores up triacylglycerols from food as lipid droplets. Fats are allocated to the formation of a new carapace during the molting stage and are transferred into eggs; as this occurs, triacylglycerol levels drop.<sup>8</sup>

Barata and colleagues observed negative effects on reproduction and survival in *Daphnia* exposed to TBT. “Our findings suggest that

TBT disrupted the normal transfer of lipids from adult to egg,” Barata says. Lipid levels in eggs from TBT-exposed females were lower than those in eggs from nonexposed females. Females exposed to TBT also retained more fat droplets after they molted. As adults, offspring of exposed females were less fit—they showed impaired survival and reduced reproduction.<sup>3</sup>

“We’ve known for a long time that TBT causes reproductive problems in *Daphnia*. This could be a mechanistic explanation,” says Gerald LeBlanc, an environmental toxicologist at North Carolina State University. LeBlanc was not involved in the study.

Previous research has suggested that TBT may disrupt certain hormonal signaling pathways in *Daphnia*.<sup>9</sup> In this study, the researchers found evidence that TBT activated signaling pathways related to molting and reproduction, presumably by increasing transcription of the retinoid X receptor (*RXR*) gene.<sup>3</sup> In vertebrates, the nuclear receptor known as peroxisome proliferator-activated receptor  $\gamma$  partners with the RXR to stimulate fat cell differentiation and lipid storage.<sup>10</sup> These receptors are known targets for TBT.<sup>11</sup>

However, LeBlanc says it would be premature to call this a model organism for the study of obesogens. “The molecular pathways that are affected [by TBT] in vertebrates don’t exist in *Daphnia*,” he says.

Bruce Blumberg, a professor of developmental and cell biology at the University of California, Irvine, agrees it may be premature to call *Daphnia* a model for the study of obesogens. Obesogens are defined as chemicals that produce weight gain by increasing the number and/or size of adipocytes or by modulating lipid metabolism.<sup>12</sup> Although lipid transfer is clearly important for fecundity of the animals, Blumberg points out that “the perturbation of lipid transfer from mother to egg in itself isn’t necessarily an obesogenic effect.” Blumberg was not involved in the current study.

Yet if chemicals that cause mammals to get fatter can also perturb lipid dynamics in an ecological context, there could be implications beyond obesity, says Michele La Merrill, a toxicologist at the University of California, Davis. “Although this study is not evaluating invertebrate obesity, it is showing some changes in lipids, and that might be a problem since lipids are important for a number of cell functions, such as membrane integrity,” she explains. La Merrill was not involved in the study.

Barata hopes the research will spur more scientists to explore the roles of known obesogens and emerging contaminants in invertebrates. He says, “There may be new mechanisms of toxicity that can affect our environment.”

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